UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,736	07/21/2003	Masahiro Okuda	Q76592	2795

23373 7590 08/20/2007

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
08/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,736	OKUDA, MASAHIRO	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-21 and 24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-21 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/16/07 has been entered.

Claims 6-21 and 24-27 are presented for continued examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8, 99-21 and 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent claims 8 and 21 recite the limitation that "the phosphatidylserine in the first reagent ranging from 30 µg/ml to 1000 µg/ml. Although this limitation was introduced when claim21 was added, it constitutes NEW MATTER because said range was never contemplated in the specification or claim, as-filed. Page 8 of the specification discloses concentration of the first preparatory reagent as "in the range from 3 to 1,000 µg/ml, preferably 30 to 100 µg/ml and

more preferably from 40 to 60 µg/ml, whereas the concentration of phosphatidylserine in the third reagent is in the range from 0.2 to 200 µg/ml, preferably from 2 to 20 µg/ml, and more preferably from 6 to 10 µg/ml." The claims as originally filed are consistent with the specification. Because the claims encompass a concentration range for phosphatidylserine that is neither contemplated nor disclosed by the as-filed disclosure, it is clear that applicant was not in possession of the full scope of the claimed subject matter at the time of filing.

Claim Rejections - 35 USC § 102

The rejection of claims 6-8, 10-14, and 19-21 under 35 U.S.C. 102(b) as being clearly anticipated by Brown (US 5,314,695) in light of Webster's Dictionary and the rejection of claims 6 and 8-13 under 35 U.S.C. 102(b) as being clearly anticipated by Smirnov et al. (1999; "Smirnov") in light of Webster's Dictionary are withdrawn since the reference does not teach the phosphatidylserine concentration which is deemed to represent NEW MATTER. Should the claims be amended to overcome the NEW MATTER rejection under 35 USC 112, first paragraph, the reinstatement of the rejections will be considered in view of other possible amendments. Therefore, Applicant's arguments regarding these rejection are considered moot at this time.

New Grounds of Rejection

Claims 6 and 8-12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Moore et al. (EP 566,333; cited in the IDS filed 10/4/05) in light of Webster's Dictionary (cited in the Office action mailed3/29/06).

Moore discloses a phospholipid (PL) reagent comprising varying amounts of phosphatidylserine (PS), phosphatidylethanolamine (PE) and phosphatidylchloline (PS) for determining clotting time of a sample. The phospholipids are synthetic, purified reagents, comprising PS, PE and PC for determining APTT and PT, thus meeting claim 6 regarding the PS source. APTT is determined by adding the PL reagent to a sample and clotting is initiated by the addition of ionic calcium. The disclosure of a source of calcium ions meets the limitations regarding a calcium ion reagent, as in instant at claims 8 and 21. Moore is silent regarding multiple calcium ion reagents. However, his disclosure is deemed to meet the claims since the claimed second and fourth reagents are identical: a source of calcium ions. There is no limitation regarding kind or concentration. Thus, a generic disclosure of calcium ions meets the second and fourth claimed reagents. APTT can be measured in the presence of an activator wherein an activator such as tissue thromboplastin which is added in the presence of calcium ions. Table II depicts the APTT values for seventeen variations of phospholipid mixtures tested against plasma samples having various clotting deficiencies including a Lupus-derived sample. Moore discloses the following species:

Run 9 comprises a specie having PS: 11.0 µg/ml; PE: 27.0 µg/ml; and PC: 128.0 µg/ml.

Run 6 comprises a specie having PS: 75.0 µg/ml; PE: 27.0 µg/ml; and PC: 128.0 µg/ml.

Run 15 comprises a specie having PS: 11.0 µg/ml; PE: 140.5 µg/ml; and PC: 72.5 µg/ml.

Run 13 comprises a specie having PS: 75.0 µg/ml; PE: 140.5 µg/ml; and PC: 72.5 µg/ml.

The disclosure of the PL mixtures for runs 6, 9, 13 and 15 meet the limitations of claims 8-10 because the disclosure of PL reagents having a concentration of 75.0 µg/ml is a specie that anticipates the claimed ranges for PS for the claimed first reagent of 30 µg/ml to 1000 µg/ml (claim 8) and 30 µg/ml to 100 µg/ml (claim 9). The disclosure of PL reagents having a PS concentration of 11.0 µg/ml is a specie that anticipates the claimed ranges for PS for the claimed third reagent of 0.20 µg/ml to 20 µg/ml (claim 8) and 2.0 µg/ml to 20 µg/ml (claim 10).

Regarding runs 6 and 9, the disclosure of PL reagent having a concentration of PE 27.0 µg/ml and PC concentration of 128.0 ug/ml is a specie that anticipates the claimed ranges for PE and PC in the first and third reagents as recited in instant claim 12: PE concentration of 0.1 to 300 µg/ml and PC concentration of 2 to 1000 µg/ml.

Likewise, for runs 13 and 15, the disclosure of PL reagent having a concentration of PE 140.5 µg/ml and PC concentration of 72.5 ug/ml is a specie that anticipates the claimed ranges for PE and PC in the first and third reagents as recited in instant claim 12: PE concentration of 0.1 to 300 µg/ml and PC concentration of 2 to 1000 µg/ml.

Thus, Moore discloses multiple preparations having PL ratios that are specie that anticipate the claimed ranges.

The disclosure by Moore falls within the scope of a kit as recited by the instant claims. According to Webster's Dictionary, a kit may be defined as: 1. a set of articles used for a particular purpose, 2. a set of parts or materials to be assembled, 3. a packaged set of related materials, or 4. a container for a kit (p. 667). Moore discloses specific PL preparations that have PS, PE and PC concentrations that are species that anticipate the claimed ranges. Thus, the disclosure

of the 17 PL preparations comprises a set of articles brought together for the purpose of testing APPT coagulation times. This disclosure meets the definition of a kit.

The disclosure by Webster's Dictionary is a supporting reference and properly used in a rejection under of U.S.C. 102 since it describes the definition of a kit. MPEP 2131.01.

Claim Rejections - 35 USC § 103

Claims 13, 21, 24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Moore et al. (EP 566,333) and Webster's Dictionary in view of Smirnov et al. (1999; previously cited).

The combined disclosure of Moore and Webster's Dictionary is discussed supra. It is again noted that Moore teaches the following PL preparations that were utilized for testing clotting times in blood samples from a lupus origin:

Run 15 comprises a specie having PS: 11.0 µg/ml; PE: 140.5 µg/ml; and PC: 72.5 µg/ml; and

Run 13 comprises a specie having PS: 75.0 µg/ml; PE: 140.5 µg/ml; and PC: 72.5 µg/ml. Moore also discloses multiple preparations having a PE content of 27 µg/ml.

The combined disclosure does not teach an additional PL preparations for testing APTT times for samples from various sources, including a Lupus source, wherein the PL content of PE and PC in the first and third reagents is PE: 1 to 30 µg/ml and PC: 20 to 100 µg/ml. Thus, Moore does not teach, for example, the following a preparations:

a modified Run 15 having PS: 11.0 µg/ml; PE: 27.0 µg/ml; and PC: 72.5 µg/ml; or

a modified run 13 having PS: 75.0 µg/ml; PE: 27.0 µg/ml; and PC: 72.5 µg/ml.

Smirnov discloses the phospholipid composition requirements for optimal prothrombin activation and factor Va inactivation by activated protein C (APC) anticoagulant and states that PE makes an important contribution to factor Va inactivation that cannot be mimicked by PS. A lupus anticoagulant immunoglobulin was more inhibitory to both prothrombinase and factor Va inactivation in the presence of PE. The degree of inhibition of APC was significantly greater and much more dependent on the phospholipid composition than that of prothrombinase. Smirnov concludes that subtle changes in the phospholipid composition of cells may control procoagulant and anticoagulant reactions differentially under both normal and pathological conditions.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a PL preparations having PS: 11.0 µg/ml; PE: 27.0 µg/ml; and PC: 72.5 µg/ml; and PS: 75.0 µg/ml; PE: 27.0 µg/ml; and PC: 72.5 µg/ml. The ordinary artisan would have been motivated to do so because both Moore and Smirnov teach that procoagulant and anticoagulant reactions are highly sensitive to PL content of the reagent used to measure same. As ruled recently,

Fact that claimed combination of elements was "obvious to try" might show that such combination was obvious under 35 U.S.C. §103, since, if there is design need or market pressure to solve problem, and there are finite number of identified, predictable solutions, person of ordinary skill in art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely product of ordinary skill and common sense, not innovation.
KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)

In the instant case, it was known that various pathological conditions, including lupus, are greatly influenced by the PL content of reagents used to test same. Moore teaches 17 different species of reagents that differ by PL content. In runs 2, 6, 9, 10 and 14, the PE concentration is 27.0 µg/ml. From Smirnov, the ordinary artisan would have known that clotting in lupus-derived

samples is sensitive to PS and PE. Thus, the ordinary artisan would have been motivated to test more PL reagents having different combinations of PL concentrations. The preparation of reagents having PS: 11.0 µg/ml; PE: 27.0 µg/ml; and PC: 72.5 µg/ml; and PS: 75.0 µg/ml; PE: 27.0 µg/ml; and PC: 72.5 µg/ml is obvious since a PE concentration of 27.0 µg/ml was used in five other reagents.

Claims 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. (EP 566,333; cited in the IDS filed 10/4/05) and Webster's Dictionary in view of Rosen et al. (US 6,395,501).

Claims 7, 13, 21, and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. (EP 566,333; cited in the IDS filed 10/4/05) and Webster's Dictionary in view of Smirnov et al. (1999; previously cited), as applied to claims 13, 21, and 24, in further view of Rosen et al. (US 6,395,501),

The disclosures of Moore and Webster's Dictionary and Moore in combination with Webster's Dictionary and Smirnov are discussed *supra*.

These references do not disclose that the coagulant activator such as tissue factor, Russell's venom, ellagic acid, kaolin or cellite can be added to the PL reagent.

Rosen discloses that phospholipids in combination with Russell's venom, ellagic acid, kaolin or silica derivatives are well known activators of the coagulation pathway and are suitable for measuring anticoagulant activity. Rosen specifically teaches that the activator is added to the PL reagent, see claims 23 and 27. Further, the source of the PL can be synthetic or natural.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ an activator such as tissue factor, Russell's venom, ellagic acid, kaolin or silica

derivatives in the phospholipid compostion taught by Moore and Webster's Dictionary or the combination of Moore, Webster's Dictionary and Smirnov. The ordinary artisan would have been motivate to do so because the various reagents are all recognized as activators of the coagulation pathway and have been used with phospholipids to measure anticoagulant activity. The ordinary artisan would have had a reasonable expectation that he or she could employ Russell's venom, ellagic acid, kaolin, silica derivatives and tissue factor as activators in a PL reagent because all been shown to activate the coagulant pathway for the purpose of measuring anticoagulant activity.

Double Patenting

Claims 6-21 and 24-27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 5, 8-18, and 21 of copending Application No. 11/050,766. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '766 are drawn to the same PL reagents and activators having overlapping concentrations as the claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Susan Hanley
Patent Examiner
AU 1651

Leon B. Lankford, Jr.
Primary Examiner
Art Unit 1651